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Effect of interparticle interaction on magnetic hyperthermia: homogeneous spatial distribution of the particles

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The paper deals with the theoretical study of the effect of magnetic interparticle interaction on magnetic hyperthermia, produced by the particles under the action of a linearly polarized oscillating field. The particles are homogeneously distributed and immobilized in a rigid medium. The supposed size of the magnetite particles is about 20–30 nm. For these particles, the characteristic time of the Neel remagnetization is much longer than the time of observation. This is why we concluded that the dissipation occurs as a result of the particle magnetic moment oscillation in the pit of energy of magnetic anisotropy.

This article is part of the theme issue 'Heterogeneous materials: metastable and non-ergodic internal structures'.

1. Introduction

Magnetic hyperthermia is a method of materials heating by embedded nano-sized ferromagnetic particles under the action of an alternating or rotating magnetic field. This effect is very promising for treating cancer and other tumour diseases. A short overview of the studies on this effect and its medical application is presented in ref. [1]. The particles, used in biomedical applications of magnetic hyperthermia, as a rule consist of magnetite of other iron oxides, because, firstly, they are not toxic; and secondly, they are relatively cheap and have magnetic moments sufficient to provide a strong link with magnetic fields, which is in laboratory and clinical conditions.

Experiments show that, being embedded in a biological environment, magnetic nanoparticles, as a rule, are tightly bound to the surrounding tissues [2,3]. Therefore, at least in the first approximation, the particles can be considered as immobilized in the tissue.

Because of the features of the internal crystal structure of ferromagnetic single-domain particles, they have one or more axes of easy magnetization—the most favourable orientation of the particle magnetic moment is along these axes. When a magnetic field directed in the opposite direction to that of the particle moment, is applied, reorientation of the moment requires transition through the potential barrier of the particle magnetic anisotropy. This process is known as the Neel remagnetization; its characteristic time is known as the Neel time of remagnetization. The moment transition through the potential barrier leads to the loss of energy and heat generation, which is roughly proportional to the Neel time. Note that this time exponentially depends on the particle volume (see ref. [4] and discussion in [1]). The majority of the known theoretical models of the magnetic hyperthermia deal with the Neel mechanism of the particle remagnetization and the heat generation (i.e. ref. [5]).

Simple estimates show that for the magnetite particles with diameters significantly less than 20 nm, the Neel time of remagnetization is much shorter than the typical time of the tissue heating (usually about half an hour) [1]. Therefore, during the heating process, the particle moment is transferred across the potential barrier many times and the models, based on the concept of the Neel remagnetization, are quite adequate to meet the physical reality. However, it was shown in experiments [6–8] that the particles with diameters of 25–30 nm are the most efficient for magnetic hyperthermia. For these particles, the time of the Neel relaxation is in the range $2.7 \times 10^3 - 3 \times 10^{12}$ s. Thus, the probability that the particle transfers the potential barrier for half an hour is very low and the concept of the Neel remagnetization, as the main mechanism of the heat production, is not adequate for the physical process.

In this case, the particle's heat production placed in an alternating magnetic field, can be induced by a small oscillation of the particle moment around the axis of easy magnetization without the transition from one favorable orientation to the opposite one. In other words, by the moment oscillations in a potential pit of the particle magnetic anisotropy without transition from one pit to another one.

This situation has been considered in previous studies [1,9]. The effect of the heterogeneous chain-like aggregates on the intensity of the heat production is studied in [1]. The work in [9] deals with a composite of the magnetically interacting particles homogeneously distributed in a medium. It was supposed that the particles' axes of easy magnetization are parallel. Physically, this means that the particles were embedded in the medium under permanent strong enough magnetic field.

In the present paper, we study the situation of the homogeneously distributed particles with random orientations of their axes of easy magnetization. The effects of magnetic interaction between the particles on the intensity of the heat production are the focus of our study.

2. Physical model and the main simplifications

We will consider a system of identical single-domain ferromagnetic particles randomly and chaotically distributed in a surrounding medium. The particles are completely immobilized; any translation and rotation of the particles is forbidden. The system is placed in a linearly polarized magnetic field, ($\boldsymbol{H} = \boldsymbol{H}_0 \cos \Omega t$). We assume that each particle has one axis of easy magnetization, as is typical for the magnetite particles (figure 1).

One of the most difficult problems in the statistical physics and physics of composite materials is accounting for the interaction between many particles (molecules) of the system. Here, in order to avoid unjustified hypotheses and theoretical constructions, we will use the well-known

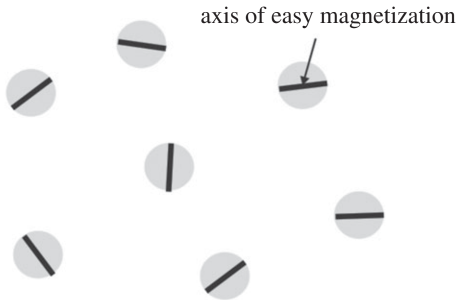

Figure 1. Sketch of the system of the particles with the random orientation of the axes of easy magentization.

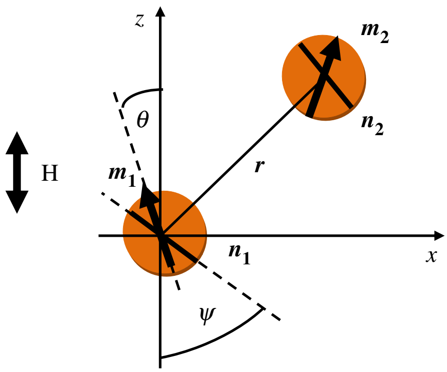

Figure 2. Sketch of the two-particles cluster in the oscillating linearly polarized field H. (Online version in colour.)

pair approximation. In other words, we will only take into account the interaction between two particles and ignore any effect from the third one.

Consider a cluster consisting of two particles, as illustrated in figure 2. Here the vectors $\boldsymbol{n}_i$ are the unit vectors of the particles' axes of easy magnetization; $\boldsymbol{m}_i$ are the unit vectors of orientation of the particles' magnetic moments.

Obviously, the heat production is especially significant in a strong magnetic field, when the thermal fluctuations of the particles' magnetic moments are negligible. In other words, the energy from the particles' interaction with the applied magnetic field is much greater than the thermal energy kT^{o}. For magnetite particles with diameter of 20 nm, this condition is true if the amplitude of the applied field exceeds $2\,\mathrm{kA\,m^{-1}}$ [1]. The typical range of the field, used in the biomedical applications of magnetic hyperthermia, is 2–15 $\mathrm{kA\,m^{-1}}$ (e.g. [6,10]). Thus, in our analysis we can ignore the fluctuations of the moments' orientations.

In this approximation, the dynamics of magnetization $\mathbf{M_i}$ of each particle can determined by the solution of the classical Landau–Lifshitz equation [11]

$$\frac{\mathrm{d}\boldsymbol{M}_i}{\mathrm{d}t} = -\gamma\mu_0[\boldsymbol{M}_i \times \boldsymbol{H}_i^{\mathrm{eff}}] - \lambda\frac{\gamma\mu_0}{M_s}[\boldsymbol{M}_i \times [\boldsymbol{M}_i \times \boldsymbol{H}_i^{\mathrm{eff}}]] \tag{2.1}$$

$$\boldsymbol{M_i} = M_s\boldsymbol{m}_i, \quad i = 1, 2.$$

Here γ is the electron hyromagnetic ratio; $\lambda \sim 0.1$ is a dimensionless dissipative parameter; $\boldsymbol{H}_i^{\mathrm{eff}}$ is an effective magnetic field, acting on the ith particle. Taking into account the classical relations [11] for this field, as well as the dipole–dipole interaction between the particles, one gets

$$\left.\begin{aligned} \boldsymbol{H}_i^{\text{eff}} &= \boldsymbol{H} + \frac{2K}{\mu_0 M_s}\boldsymbol{n}(\boldsymbol{m}\cdot\boldsymbol{n}) + \boldsymbol{H}_i^{dd} \\ \boldsymbol{H} &= \boldsymbol{H}_0 \cos \varOmega t \\ \text{and} \qquad \boldsymbol{H}_i^{\text{dd}} &= \frac{1}{4\pi}\frac{3(\boldsymbol{m}_j\cdot\boldsymbol{r})r - \boldsymbol{m}_j r^2}{r^5}, \quad i\neq j,\ i,j=1,2. \end{aligned}\right\} \tag{2.2}$$

Here $\boldsymbol{H}_i^{dd}$ is the dipole field, which is created by the jth particle in the position of the ith one; $\boldsymbol{r}$ is the radius-vector, linking the centres of the particles, K is the parameter of the particle magnetic anisotropy; M_s is the saturation magnetization of the particle; μ_0 is the vacuum magnetic permeability.

For convenience, let us introduce the dimensionless time τ, angular frequency ω and dimensionless effective field $\boldsymbol{h}^{\text{eff}}$ as

$$\tau = \frac{t}{t_0}, \omega = \varOmega t_0,\ \boldsymbol{h}_i^{\text{eff}} = \frac{\boldsymbol{H}_i^{\text{eff}}}{M_s} = \boldsymbol{h}_w + \beta\boldsymbol{n_i}(\boldsymbol{m_i}\cdot\boldsymbol{n_i}) + \boldsymbol{h}_i^{dd}, \tag{2.3}$$

where

$$\begin{aligned} \boldsymbol{h}_w &= h_0 \cos \omega\tau \\ \boldsymbol{h}_i^{\text{dd}} &= \frac{d^3}{24}\frac{3(\boldsymbol{m}_j\cdot\boldsymbol{r})r - \boldsymbol{m}_j r^2}{r^5}, i\neq j \quad i,j=1,2 \\ \text{and} \qquad t_0 &= \frac{1}{\mu_0\gamma M_s} \approx 9\cdot 10^{-10} s; \beta = \frac{2K}{\mu_0 M_s^2} \approx 0.11,\ h_0 = \frac{\boldsymbol{H}_0}{M_s}. \end{aligned}$$

Here d is diameter of the particle.

The estimates of t_0 and β are given here for magnetite particles, taking into account the values $K \approx 14\,\text{kJ m}^{-3}$ and $M_s \approx 4.5 \times 10^2\,\text{kA m}^{-1}$ [12].

By using the dimensionless variations (2.3), one can rewrite equation (2.1) in the form:

$$\frac{\mathrm{d}\boldsymbol{m}_i}{\mathrm{d}\tau} = -[\boldsymbol{m}_i \times \boldsymbol{h}_i^{\text{eff}}] - \lambda[\boldsymbol{m}_i \times [\boldsymbol{m}_i \times \boldsymbol{h}_i^{\text{eff}}]], \quad i=1,2. \tag{2.4}$$

Relations (2.4) present a system of nonlinear differential equations with respect to the components of the unit vectors $\boldsymbol{m_i}$. In the general case, this system can be solved only numerically.

In order to get some analytical results, we will restrict ourselves to the relatively weak fields, when the inequality $\mu_0 M_s H_0 < K$ is held. By using here the noted values of K and M_s, we come to the restriction for the field amplitude $H_0 < 20\,\text{kA m}^{-1}$. Let us remember that the typical strengths of the field, used in medical applications of magnetic hyperthermia, are in the region of $15\,\text{kA m}^{-1}$, i.e. they satisfy this inequality.

The intensity W of heat production (the heat production per unit of time in a unit volume of the system) can be determined on the basis of the general relation of thermodynamics of magnetizable media [13] (see also, [14]):

$$W = -\frac{\mu_0}{T}\varPhi\int_0^T M_z(t)\frac{\mathrm{d}H}{\mathrm{d}t}\mathrm{d}t. \tag{2.5}$$

Here $\varPhi$ is the volume concentration of the particles, T is time much greater than that of the field alternation; $\boldsymbol{M}$ is the magnetization of an arbitrary (say, the first) particle, shown in figure 2;

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M_z is a component of $\boldsymbol{M}$ along the oscillating field $\mathbf{H}$. By using the dimensionless variables (2.3) and $\boldsymbol{H}=\boldsymbol{H}_0\cos\Omega t$, we can rewrite equation (2.5) as

$$\left.\begin{aligned} W&=\mu_0\Phi\frac{M_s^2}{t_0}w,\\ w&=-\frac{1}{\Theta}\int_0^{\Theta} m_z\frac{\mathrm{d}h}{\mathrm{d}\tau}\mathrm{d}\tau=\frac{\omega h_0}{\Theta}\int_0^{\Theta} m_z\sin\omega\tau\,\mathrm{d}\tau\\ \text{and}\qquad m_z&=\frac{M_z}{M_s},\quad \Theta=\frac{T}{t_0}.\end{aligned}\right\}\tag{2.6}$$

Here w is a dimensionless intensity of the heating effect per one particle.

Thus, in order to determine the intensity W of the heat production, one needs to solve the system of equations (2.4), to find the component m_z of the unit vector $\boldsymbol{m}$ of the first particle and to calculate the integral (2.6).

3. Mathematical model

Let us begin with the approximation of the interparticle interaction particles in three-dimensional easy magnetization under the influence of linearly polarized magnetic field, i.e. consider the system (2.4) under the assumption $\boldsymbol{h}_i^{dd}\neq 0$. Equation (2.4) reads:

$$\left.\begin{aligned} \frac{\mathrm{d}\boldsymbol{m}}{\mathrm{d}\tau}&=-[\boldsymbol{m}\times\boldsymbol{h}^{\mathrm{eff}}]-\lambda[\boldsymbol{m}\times[\boldsymbol{m}\times\boldsymbol{h}^{\mathrm{eff}}]],\\ \boldsymbol{h}^{\mathrm{eff}}&=\boldsymbol{h}_w+\beta\boldsymbol{n}(\boldsymbol{m}\cdot\boldsymbol{n})+\boldsymbol{h}_i^{dd}\\ \text{and}\qquad \boldsymbol{h}_w&=h_0\cos\omega\tau.\end{aligned}\right\}\tag{3.1}$$

We will use the Cartesian coordinate system with the axis Oz aligned along the direction of the field $\boldsymbol{H}$, and axis O_x aligned in the plane, formed by the vectors $\boldsymbol{H}$ and $\boldsymbol{n}_1$ (figure 2). It will be convenient also to introduce the spherical coordinate for the vector $\boldsymbol{m}$ for two particles as

$$m_{x_i}=\sin\theta_{\mathrm{i}}\cos\varphi_i,\quad m_{y_i}=\sin\theta_i\sin\varphi_i,\quad m_{z_i}=\cos\theta_i.\tag{3.2}$$

Here $i=1{,}2$ is the number of particles; θ_i and φ_i are the polar and azimuth angles of the particles, respectively.

Let x,y,z be the Cartesian coordinates of the vector $\boldsymbol{r}$, linking centres of the particles, shown in figure 2.

In the spherical coordinate system (3.2), the vector equation (3.1) can be presented as

$$\left.\begin{aligned} \frac{\mathrm{d}\theta_i}{\mathrm{d}t}&=(-\sin\varphi_i+\lambda\cos\theta_i\cos\varphi_i)h_{x_1}^{\mathrm{eff}}+(\cos\varphi_i+\lambda\cos\theta_i)h_{y_1}^{\mathrm{eff}}-\lambda\sin\theta_1 h_{z_1}^{\mathrm{eff}}\\ \text{and}\qquad \sin\theta_i\frac{\mathrm{d}\varphi_i}{\mathrm{d}t}&=-(\cos\theta_i\cos\varphi_i+\lambda\sin\varphi_i)h_{x_1}^{\mathrm{eff}}+(\lambda\cos\varphi_i-\cos\theta_i\sin\varphi_i)h_{y_1}^{\mathrm{eff}}+\sin\theta_i h_{z_1}^{\mathrm{eff}}\end{aligned}\right\}\tag{3.3}$$

Here,

$$\begin{aligned} h_{z_i}^{\mathrm{eff}}&=h_0\cos\omega\tau+\beta n_{z_i}(n_{z_i}\cos\theta_i+n_{x_i}\sin\theta_i\cos\varphi_i+n_{yi}\sin\theta_i\sin\varphi_i)+h_{z_i}^{dd}\\ h_{x_i}^{\mathrm{eff}}&=\beta n_{x_i}(n_{z_i}\cos\theta_i+n_{x_i}\sin\theta_i\cos\varphi_i+n_{y_i}\sin\theta_i\sin\varphi_i)+h_{x_i}^{dd}\\ h_{y_i}^{\mathrm{eff}}&=\beta n_{y_i}(n_{z_i}\cos\theta_i+n_{x_i}\sin\theta_i\cos\varphi_i+n_{y_i}\sin\theta_i\sin\varphi_i)+h_{y_i}^{dd},\ i=1,2.\end{aligned}$$

Note, in the chosen Cartesian coordinate system $n_{y1}=0$.

The components of the field of the dipole–dipole interaction between the particles is

$$\left.\begin{aligned} h_{z_i}^{dd} &= \frac{d^3}{24r^5}(3z(z\cos\theta_j + x\sin\theta_j\cos\varphi_j + y\sin\theta_j\sin\varphi_j) - r^2\cos\theta_j), \\ h_{x_i}^{dd} &= \frac{d^3}{24r^5}(3x(z\cos\theta_j + x\sin\theta_j\cos\varphi_j + y\sin\theta_j\sin\varphi_j) - r^2\sin\theta_j\cos\varphi_j) \\ \text{and}\quad h_{y_i}^{dd} &= \frac{d^3}{24r^5}(3y(z\cos\theta_j + x\sin\theta_j\cos\varphi_j + y\sin\theta_j\sin\varphi_j) - r^2\sin\theta_j\sin\varphi_j), \end{aligned}\right\} \tag{3.4}$$

where

$$r = \sqrt{x^2 + x^2 + z^2},\ i \neq j,\ i, j = 1, 2$$

For convenience, we present the unit vectors $\boldsymbol{n_i}$ of the particles easy magnetization as

$$n_{z_i} = \cos\psi_i, n_{xi} = \sin\psi_i\cos\phi_i, \quad n_{yi} = \sin\psi_i\sin\phi_{\mathrm{i}}, \tag{3.5}$$

where ψ_i and ϕ_i are the polar and azimuth angles of $\boldsymbol{n_i}$, respectively**.** In the chosen coordinate system $\phi_1 = 0$.

By using the dimensionless variations (2.3), one can rewrite the inequality $\mu_0 M_s H_0 < K$ as $h_0 < \beta$. Let us suppose that the strong inequality $h_0 \ll \beta$ is held. In the absence of the applied magnetic field ($h_0 = 0$), the vector $\boldsymbol{m_i}$ must be aligned along the vector $\boldsymbol{n}_i$ of the axis of the ith particle's easy magnetization. This means that without the field the equalities $\theta_i = \psi_i, \varphi_i = \phi_i$ must be held.

Because of the strong inequality $h_0 \ll \beta$, the field induced deviation of the vector $\boldsymbol{m_i}$ from the axis $\boldsymbol{n}_i$ of the particle easy magnetization must be small. In the other words, one can put $|\varphi| \ll 1$;

$$\left.\begin{aligned} \theta_i &= \psi_i + \varepsilon_i, |\varepsilon_i| \ll 1 \\ \text{and}\quad \varphi_i &= \phi_i + \sigma_i, |\sigma_i| \ll 1. \end{aligned}\right\} \tag{3.6}$$

Let us discuss briefly the further calculations. By using (3.6), keeping only terms with small variation, one can rewrite the system (3.3) in the linear approximation with respect to ε_i and $\sigma_{i,}$ in the form:

$$\left.\begin{aligned} \frac{\mathrm{d}\varepsilon_1}{\mathrm{d}\tau} + A_{\varepsilon_1}\varepsilon_1 + A_{\varepsilon_2}\varepsilon_2 + A_{\sigma_1}\sigma_1 + A_{\sigma_2}\sigma_2 &= -\lambda h_0\sin\psi_1\cos\omega\tau + A_{c1}, \\ \frac{\mathrm{d}\varepsilon_2}{\mathrm{d}\tau} + A_{\varepsilon\varepsilon_1}\varepsilon_1 + A_{\varepsilon\varepsilon_2}\varepsilon_2 + A_{\sigma\sigma_1}\sigma_1 + A_{\sigma\sigma_2}\sigma_2 &= -\lambda h_0\sin\psi_1\cos\omega\tau + A_{c2}, \\ \sin\psi_1\frac{\mathrm{d}\sigma_1}{\mathrm{d}\tau} + B_{\sigma_1}\sigma_1 + B_{\sigma_2}\sigma_2 + B_{\varepsilon_1}\varepsilon_1 + B_{\varepsilon_2}\varepsilon_2 &= h_0\sin\psi_2\cos\omega\tau + B_{c1} \\ \text{and}\quad \sin\psi_2\frac{\mathrm{d}\sigma_2}{\mathrm{d}\tau} + B_{\sigma\sigma_1}\sigma_1 + B_{\sigma\sigma_2}\sigma_2 + B_{\varepsilon\varepsilon_1}\varepsilon_1 + B_{\varepsilon\varepsilon_2}\varepsilon_2 &= h_0\sin\psi_2\cos\omega\tau + B_{c2}. \end{aligned}\right\} \tag{3.7}$$

Here,

$$A_{\varepsilon_1} = 2\lambda\beta + \frac{d^3}{24r^5}[\lambda[(3x^2 + 3xy - r^2)\sin\psi_1 + 6xz + 3yz] + (3xy + 3y^2 - r^2)\cos\psi_1 + 3yz],$$

$$A_{\varepsilon_2} = -\frac{\lambda d^3}{24r^5}[\lambda[(3xy + 3y^2 - r^2)\cos\psi_1 - 3yz\sin\psi_1 - 3xz + 3z^2] - 3xz\sin\psi_2 + 3y^2 - r^2],$$

$$A_{\varepsilon\varepsilon_1} = -\frac{d^3}{24r^5}[-\lambda(3yz + 3xz - 3z^2 + r^2) + 3xz - 3x^2 - 3yz + r^2]$$

$$A_{\varepsilon\varepsilon_2} = -\lambda\beta(1 + \sin\psi_2 + \cos\psi_2) + \frac{\lambda d^3}{24r^5}[3xz\cos\psi_1 + (3x^2 - r^2)\sin\psi_1 + 3yz + 3xy + 3xz + 3z^2 - 2r^2]$$

$$A_{\sigma_1} = \beta\sin\psi_1 + \frac{d^3}{24r^5}[3xz\cos\psi_2 + 3x^2 + 3xy - r^2]$$

$$A_{\sigma_2} = \frac{d^3}{24r^5}[\lambda[(3x^2 + 3y^2 - r^2)\cos\psi_1 + (3yz - 3xz)\sin\psi_1] + (3xy + 3y^2 + r^2)\cos\psi_1]$$

$$A_{\sigma\sigma_1} = -\frac{d^3}{24r^5}[3y^2 - 3xy + \lambda(3y^2 + 3yz)],$$

$$A_{\sigma\sigma_2} = \lambda\beta + \beta(\cos\phi_2 + \sin\phi_2) + \frac{d^3}{24r^5}[\lambda(3xz\cos\psi_1 + (3x^2 - r^2)\sin\psi_1) + 3x^2 + 3yz + 3xy - 2r^2]$$

$$A_{c1} = \frac{d^3}{24\pi r^5}[\lambda[(-3z^2 - 3xz - 3yz + r^2)\sin\psi_1 + (3x^2 + 6xy + 3y^2 - 2r^2)\cos\psi_1] + 3yz\cos\psi_2 + 3yz + 3y^2 - r^2],$$

$$A_{c2} = \lambda\beta(\cos\psi_1 - 1) + \beta(\cos\phi_2 - \sin\phi_2) + \frac{d^3}{24r^5}[\lambda(3xy - r^2) + 3xy - 6xz - 6z^2 + r^2],$$

and

$$B_{\varepsilon_1} = -2\beta - \frac{d^3}{24r^5}[(3x^2 + 3xy - r^2)\sin\psi_1 + 6xz + 3yz],$$

$$B_{\varepsilon_2} = -\frac{d^3}{24r^5}[\lambda(3y^2 - 3yz\sin\psi_2 - r^2) - 3xy\cos\psi_2 + 3yz\sin\psi_1 + 3xz - z^2 - r^2],$$

$$B_{\varepsilon\varepsilon_1} = \frac{d^3}{24r^5}[\lambda(3x^2 - 3xz + 3xy - r^2) + (3x^2 - r^2)\cos\psi_1 - 3xz\sin\psi_1 - 3xz + 3z^2 + r^2],$$

$$B_{\varepsilon\varepsilon_2} = -2\beta - \beta\cos\psi_2 - \frac{d^3}{24r^5}[(3xz + 3yz)\cos\psi_1 + (3x^2 + 3xy - 2r^2)\sin\psi_1 + 3z^2 - r^2],$$

$$B_{\sigma_1} = \lambda\beta\sin\psi_1 + \frac{\lambda d^3}{24r^5}[3xz\cos\psi_1 + 3x^2 + +3xy - r^2],$$

$$B_{\sigma_2} = \frac{d^3}{24r^5}[\lambda(3xy + 3y^2 + r^2) + (3xy - 3x^2)\cos\psi_1 - (3yz - 3xz)\sin\psi_1],$$

$$B_{\sigma\sigma_1} = \frac{d^3}{24r^5}[3xy\sin\psi_1 - 3yz],$$

$$B_{\sigma\sigma_2} = -\beta + \lambda\beta(\cos\phi_2 + \sin\phi_2) + \frac{d^3}{24r^5}[\lambda(3x^2 + 3yz + 3xy - 2r^2) - 3xz\cos\psi_1 + (3x^2 - r^2)\sin\psi_1],$$

$$B_{c1} = \frac{d^3}{24\pi r^5}[\lambda(3yz\cos\psi_2 + 3xy + 3y^2 - r^2) + (3z^2 + 3xz + 3yz - r^2)\sin\psi_1 - 3x^2 - 3xy + r^2],$$

$$B_{c2} = \lambda\beta(\cos\phi_2 - 1) + \frac{d^3}{24r^5}[\lambda(3xy - 3xz - 3x^2 - r^2) - 3xz\cos\psi_1 - (3xy - r^2)\sin\psi_1 + 3z^2 + 3xz - r^2],$$

The term proportional d^3 corresponds to the dipole–dipole interparticle interaction of the particles.

As is usual in the solution of linear differential equations, it is convenient to use in (3.7) the complex exponent $e^{i\omega t}$ instead of $\cos\omega t$.

For the further calculations, we will need the angle ε_1, which can be presented as

$$\varepsilon_1 = (\chi_1' + i\chi_1'')h_0 e^{i\omega t}\sin\psi_1, \tag{3.8}$$

where χ_i' and χ_i'' are relative real and imaginary parts of the particle dynamic susceptibility, estimated in the frames of the pair interaction between the particles.

Substituting ((3.2), (3.5), (3.6)) into (2.6), in the linear approximation with respect to ε_1, we get

$$w = -\frac{\omega h_0}{\Theta}\sin\psi_1\int_0^{\Theta}\varepsilon_1(\tau)\sin\omega\tau\,\mathrm{d}\tau = \frac{\omega {h_0}^2}{2}\chi_1''\sin^2\psi_1. \tag{3.9}$$

Note that imaginary susceptibility χ_1'' depends on the components x,y,z of the dimensionless vector $\boldsymbol{r}$ as well as on the angles ψ_2,ϕ_2 of orientation of the vector $\boldsymbol{n}_2$. The physical meaning has the averaged, over all these variables, value $\langle w\rangle$of the intensity $w(\boldsymbol{r},\boldsymbol{n}_1,\boldsymbol{n}_2)$.

In order to average, we will follow the method suggested in [9]. Namely, we present the susceptibility χ_1'' as

$$\chi_1'' = \chi_{10}'' + \delta\chi_1''. \tag{3.10}$$

Here χ_{10}'' is the imaginary susceptibility calculated in the approximation of non-interacting particles. Direct calculations give [1]

$$\chi'' = \lambda\omega\frac{\beta^2(1+\lambda^2)+\omega^2}{\left[\beta^2(1+\lambda^2)-\omega^2\right]^2+4(\beta\lambda\omega)^2}.$$

The magnitude $\delta\chi_1''$ reflects the contribution of the interparticle interaction to the susceptibility χ_1''. This part of the susceptibility depends on the variables x,y,z, ψ_2,ϕ_2 and must be averaged over them.

Let us denote a distribution function over all relative positions of the particles as $g(r)$ and suppose that the normalization condition $g\to 1$, at $r\to\infty$ is held. Note that in an isotropic medium the function g depends only on the absolute value r of the radius-vector $\boldsymbol{r}$.

On the basis of the standard considerations of statistical physics (e.g. [15]), one can get the following relation for the average magnitude of the susceptibility:

$$\langle\chi''\rangle = \frac{2}{3}\left[\chi''_{10} + \frac{\Phi}{4\pi v_p}\int\delta\chi''(\boldsymbol{r},\psi_2,\phi_2)g(r)\sin\psi_2\mathrm{d}\psi_2\mathrm{d}\phi_2\mathrm{d}\boldsymbol{r}\right] \tag{3.11}$$

$$0\le\psi_2\le\pi;\, 0\le\phi_2\le 2\pi;\, r\ge d$$

Here $v_p = (\pi/6)d^3$ is the particle volume. The results obtained from averaging the function $\sin^2\psi_1$ over all ψ_1 at the chaotic orientations of the vector $\boldsymbol{n}_1$:

$$\langle\sin^2\psi_1\rangle = \frac{1}{2}\int_0^{\pi}\sin^3\psi_1\mathrm{d}\psi_1 = \frac{2}{3}$$

is taken into account.

In the frame of the pair approximation, one can use the simplest form

$$g(r) = \begin{cases} 0, & r<d \\ 1, & r\ge d, \end{cases} \tag{3.12}$$

of the distribution function. This form takes into account the impossibility of the particles' interpenetration.

Note that the function $\delta\chi''(\boldsymbol{r},\boldsymbol{n}_2)$ includes energy of the dipole–dipole interaction between the particles (see equations ((3.3) and (3.4))) and, at $r\to\infty$, linearly depends on the terms (3.4) of this interaction. It is well known that integrals such as (3.11) over the potential of the dipole–dipole interaction above the vector r converge conditionally, because of slow, i.e. $1/r^3$, decay of the potential. In other words, this integral depends on the order of integration over components of the vector $\boldsymbol{r}$.

Integrating in (3.11) over $\boldsymbol{r}$, as in [9], we will use an approach suggested in [16] and successfully used for calculations of thermodynamic characteristics of systems of particles with the dipole–dipole interaction. The main idea is that the integration over $\boldsymbol{r}$ in relations such as (3.11) (i.e. over the potential of the dipole–dipole interaction) must be taken over a cylinder, infinitely elongated in the direction of the field $\mathbf{H}$, in which the particles are placed. The physical justification of this

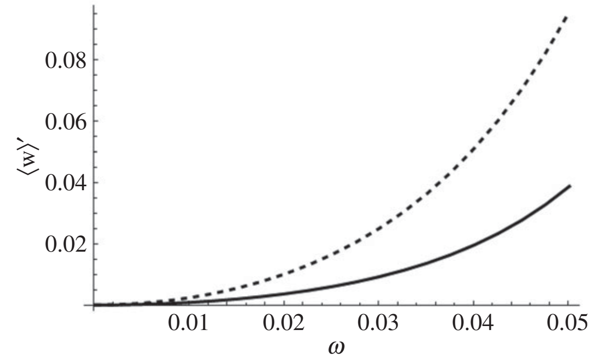

Figure 3. Dimensionless intensity $\langle w\rangle' = (3/h_0^2)\langle w\rangle$ of the heat production versus the dimensionless frequency ω of the magnetic field alternation. Solid curve—approximation of the non-interacting particles ($\Phi = 0$ in equation (3.15)); and dashed curve calculated at $\Phi = 1\%$. Other parameters of the system $\lambda = 0.1$; $\beta = 0.11$; $d = 10$ nm.

approach is that this shape of the region of integration creates equality of the acting field **H** to the field inside this region.

To this end, we introduce a cylindrical coordinate system with its origin in the centre of the first particle, illustrated in figure 2; the polar axis Oz, aligned along the direction of the field **H**; the distance ρ of the centre of the second particle from the axis Oz and the polar angle ϑ. In this coordinate system, the integral over $\boldsymbol{r}$ in (3.11) can be presented as

$$\int \delta\chi''(\boldsymbol{r})g(r)\mathrm{d}\boldsymbol{r} = 2\int_{2\pi}^{2\pi}\int_0^{\infty}\int_{\sqrt{d^2-\rho^2}}^{\infty}\delta\chi''(\boldsymbol{r})\mathrm{d}z\rho\mathrm{d}\rho\mathrm{d}\vartheta + \int_0^{2\pi}\int_d^{\infty}\int_{-\infty}^{\infty}\delta\chi''(\boldsymbol{r})\mathrm{d}z\rho\mathrm{d}\rho\mathrm{d}\vartheta. \tag{3.13}$$

It should be stressed that the order of integration over the coordinates z and ρ is of principal importance here. Change of this order leads to a change of sign of the integral, and thus to a qualitative change in the conclusion on the effect of the interparticle interaction on heat production.

It is convenient to rewrite the relation (3.13) in the following form:

$$\int \delta X''(\boldsymbol{r})g(r)\mathrm{d}\boldsymbol{r} = Jd^3,$$

$$J(\psi_2,\phi_2) = 2\int_0^{2\pi}\int_0^{\infty}\int_{\sqrt{1-\varrho^2}}^{\infty}\delta\chi(\boldsymbol{r},\psi_2,\phi_2)\mathrm{d}\xi\varrho\mathrm{d}\varrho\mathrm{d}\phi + \int_0^{2\pi}\int_1^{\infty}\int_{-\infty}^{\infty}\delta X''(\boldsymbol{r},\psi_2,\phi_2)\mathrm{d}\xi\varrho\mathrm{d}\varrho\mathrm{d}\vartheta$$

$$\xi = \frac{z}{d},\ \varrho = \frac{\rho}{d}. \tag{3.14}$$

Combining equations ((3.9), (3.11), (3.12)) and (3.14), one gets

$$\langle w\rangle = \frac{\omega h_0^2}{3}\left[\chi_{10}'' + \frac{3\Phi}{2\pi^2}\int J(\psi_2,\phi_2)\sin\psi_2\mathrm{d}\psi_2\mathrm{d}\phi_2\right]. \tag{3.15}$$

The first term in the brackets corresponds to the effect of a single particle, the second one reflects the effect of the interparticle interaction.

4. Results

Some results of calculations of the average dimensionless intensity $\langle w\rangle$ of the heat production per one particle are presented in figure 3. The results demonstrate that magnetic interparticle interaction enhances the thermal effect. Note that a similar conclusion has been made in ref. [9] for the particles with parallel (not arbitrary) orientation of the axes of the particles' easy magnetization. Contrary to that, results of ref. [1] show that magnetic interaction of the particles, united into chain-like aggregate, reduce the effect in the range of relatively small frequencies, corresponding to figure 3. Therefore, the influence of the interparticle interaction on the heat production in magnetic hyperthermia depends qualitatively on the morphology of the particles' disposition in the current media.

5. Conclusion

We present the results of a theoretical study of magnetic hyperthermia produced by single-domain magnetic particles chaotically distributed and immobilized in a rigid medium. The axes of the particles' easy magnetization have random orientation. The system is placed in a linearly polarized magnetic field; the energy of the particle Zeeman interaction with the field is much less than the energy of the particle magnetic anisotropy. Magnetic interaction between the particles is taken into account in the frames of mathematically regular approximation of pair interaction, which can be considered a strict approach if the particle concentration is small enough. Our results show that in these systems with a chaotic spatial distribution of the particles, magnetic interparticle interaction can significantly enhance the thermal effect. By contrast, the results of [1] demonstrate that, in the case of the particles united in heterogeneous chain-like aggregates, this interaction weakens the heat production. Therefore, the effect of interparticle interaction on heat production in magnetic hyperthermia is determined by the morphology of the particles' spatial disposition. This conclusion must be taken into account in the clinical usage of this phenomenon.

Data accessibility. This article has no additional data.

Competing interests. We have no competing interests.

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